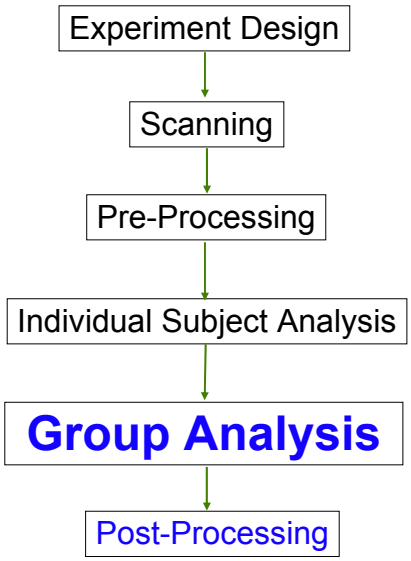
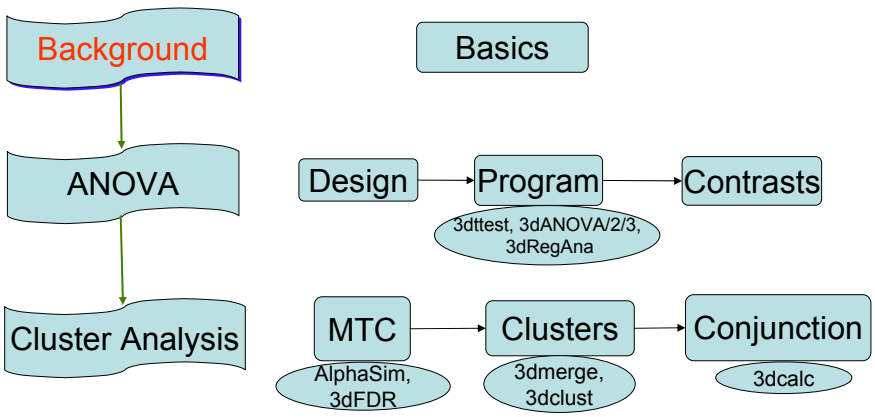
FMRI Analysis

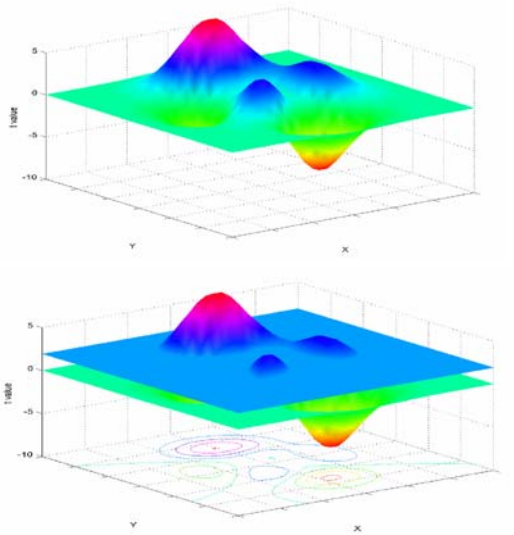


Group Analysis



Basics: Null hypothesis significance testing (NHST)

- *Main function of statistics is to get more information into the data*
- Null and alternative hypotheses
  - **H_0**: nothing happened vs. **H_1**: something happened
- Dichotomous decision
  - Rejecting H_0 at a significant level α (e.g., 0.05)
  - Subtle difference
    - *Traditional*: Hypothesis holds until counterexample occurs;
    - *Statistical*: discovery holds when a null hypothesis is rejected with some statistical confidence
  - Topological landscape vs. binary world



Basics: Null hypothesis significance testing (NHST)

- Dichotomous decision
  - **Conditional probability** $P(\text{reject } H_0 \mid H_0) = \alpha \neq P(H_0)$!
  - 2 types of errors and power
    - Type I error = $\alpha = P(\text{reject } H_0 \mid H_0)$
    - Type II error = $\beta = P(\text{accept } H_0 \mid H_1)$
    - Power = $P(\text{accept } H_1 \mid H_1) = 1 - \beta$

Justice System: Trial

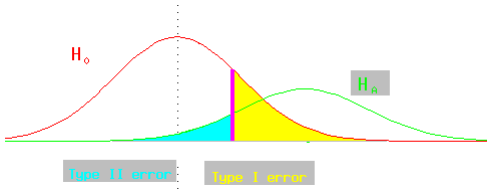
	Defendant Innocent	Defendant Guilty
Reject Presumption of Innocence (Guilty Verdict)	Type I Error	Correct
Fail to Reject Presumption of Innocence (Not Guilty Verdict)	Correct	Type II Error

Statistics: Hypothesis Test

	H_0 True	H_0 False
Reject H_0	Type I Error	Correct
Fail to Reject H_0	Correct	Type II Error

• Basics: Null hypothesis significance testing (NHST)

↙Compromise and strategy



➢Lower type II error under fixed type I error

➢Control false + while gaining as much power as possible

➢Check **efficiency** (power) of design with **`RSFgen`** before scanning

↙Typical misinterpretations*)

➢Reject H_0 → Prove or confirm a theory (alternative hypothesis)! (wrong!)

➢*P*(reject H_0 | H_0) = *P*(H_0) (wrong!)

➢*P*(reject H_0 | H_0) = Probability if the experiment can be reproduced (wrong!)

*) *Cohen, J., "The Earth Is Round (p < .05)" (1994), American Psychologist, 49, 12 997-1003*

• Basics: Null hypothesis significance testing (NHST)

- Controversy: Are humans cognitively good intuitive statisticians?
- Quiz: HIV prevalence = 10^{-3}, false + of HIV test = 5%, power of HIV test ~ 100%.
  - ↙ P(HIV+ | test+) = ?

$$P(HIV+|test+)=\frac{P(test+|HIV+)P(HIV+)}{P(test+|HIV+)P(HIV+)+P(test+|HIV-)P(HIV-)}=\frac{1.0\times10^{-3}}{1.0\times10^{-3}+0.05\times(1-10^{-3})}\approx 0.02$$

- Keep in mind
  - ↙ Better plan than sorry: Spend more time on experiment design (power analysis)
  - ↙ More appropriate for detection than sanctification of a theory
    - ➢ Modern phrenology?
  - ↙ Try to avoid unnecessary overstatement when making conclusions
  - ↙ Present graphics and report % signal change, standard deviation, confidence interval, …
  - ↙ Replications are the best strategy on induction/generalization
    - ➢ Group analysis

Quiz

A researcher tested the null hypothesis that two population means are equal (H_0: $\mu_1 = \mu_2$). A *t*-test produced p=0.01. Assuming that all assumptions of the test have been satisfied, which of the following statements are true and which are false? Why?

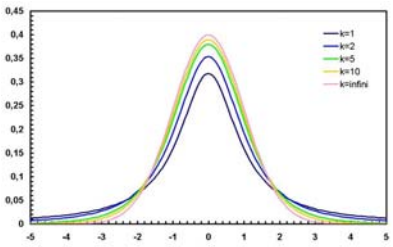
1. There is a 1% chance of getting a result even more extreme than the observed one when H_0 is true.
2. There is a 1% likelihood that the result happened by chance.
3. There is a 1% chance that the null hypothesis is true.
4. There is a 1% chance that the decision to reject H_0 is wrong.
5. There is a 99% chance that the alternative hypothesis is true, given the observed data.
6. A small *p* value indicates a large effect.
7. Rejection of H_0 confirms the alternative hypothesis.
8. Failure to reject H_0 means that the two population means are probably equal.
9. Rejecting H_0 confirms the quality of the research design.
10. If H_0 is not rejected, the study is a failure.
11. If H_0 is rejected in Study 1 but not rejected in Study 2, there must be a moderator variable that accounts for the difference between the two studies.
12. There is a 99% chance that a replication study will produce significant results.
13. Assuming H_0 is true and the study is repeated many times, 1% of these results will be even more inconsistent with H_0 than the observed result.

Adapted from Kline, R. B. (2004). Beyond significance testing. Washington, DC: American Psychological Association (pp. 63-69). Dale Berger, CGU 9/04

- *Hint: Only 2 statements are true*

Basics: Student's *t*

- Background
  - Gossett, 1908, Guinness brewing company, Dublin
  - Named arbitrarily by R. A. Fisher
  - Bell-shaped, but more spread out
  - DF: asymptotically approaches N(0,1) as DF→∞
  - One tail or two?
  - Special case of *F*: $t^2(n) = F(1, n)$

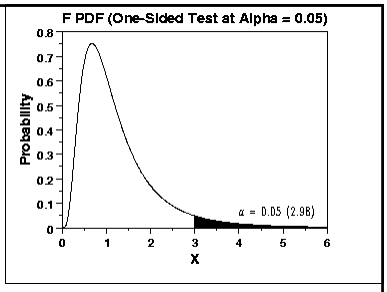


- Usages: one-sample, two-sample, and paired *t*
  - **One-sample**
    - Effect of a condition at group level
    - Group Mean relative to Standard Error of group Mean (SEM)

$$T = \frac{\overline{X}_n - \mu}{S_n/\sqrt{n}} \qquad S_n^2 = \frac{1}{n-1}\sum_{i=1}^{n}\left(X_i - \overline{X}_n\right)^2$$

  - **Two-sample**
    - Comparison between 2 groups
    - (Difference of group means)/(Pooled SEM)
  - **Paired**
    - Comparison between 2 conditions at group level
    - (Difference of conditions)/(SEM of individual differences)
  - Contrast and general linear test in regression and ANOVA
    - `3dDeconvolve`, `3dRegAna`, `3dfim/+`, `3dttest`, `3dANOVA/2/3`
- Assumptions
  - Gaussian and Sphericity: heteoscedasticity in two-sample *t*

Basics: *F*



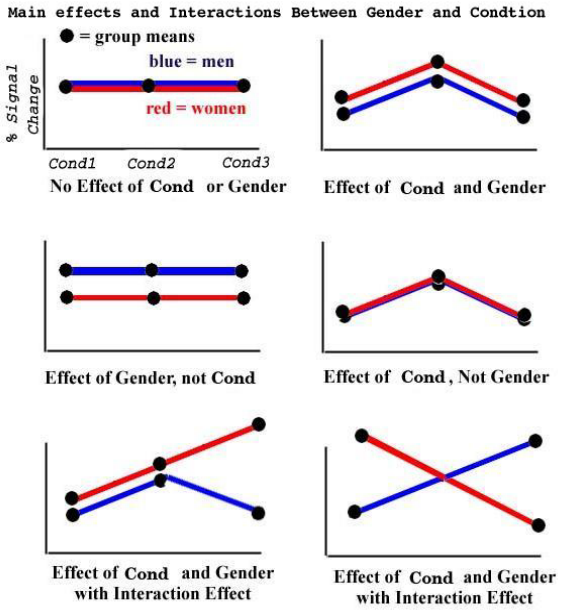
- Background
  - Named after Sir R. A. Fisher
  - Ratio of two Chi-square distributions
  - Two parameters, $F(n_1, n_2)$
  - One tail or two?
  - t is a special case of F: $t^2(n) = F(1, n)$
- Usages:
  - Two or more samples have the same variance?
    - ANOVA: Main effects and interactions
  - What proportion of variation (effect) in the data is attributable to some cause?
    - Regression: Partial F and glt in **`3dRegAna, 3dDeconvolve`**
- Assumptions
  - Gaussian
  - Sphericity
    - More than two conditions
    - Basis function modeling

Basics: ANOVA

- Factor and level
  - Dependant and independent variable
  - Factors: categorizing variables, e.g., subject category and stimulus class
    - Subject categories: sex, genotypes, normal vs. patient
    - Stimulus categories: 4 (2x2) stimuli, object (human vs. tool), res (motion vs. points)
  - Levels: nominal (qualitative) values of a factor
    - Object: human and tool; Resolution: high and low
- Fixed/random factor
  - Fixed: specific levels of a factor are of interest
  - Random (usually subject in fMRI)
    - Each level (a specific subject) of the factor is not of interest
    - But factor variance should be accounted for (cross-subject variation)
    - Random-effect model
- Different terminology for Factorial (crossed)/nested
  - Count subject as a random factor (statisticians); Random-effect model
  - Within-subject (repeated measures) / between-subjects (psychologists)
  - Crossed and nested designs
- Group analysis
  - Make general conclusions about some population
  - Partition/untangle data variability into various sources (effect → causes)

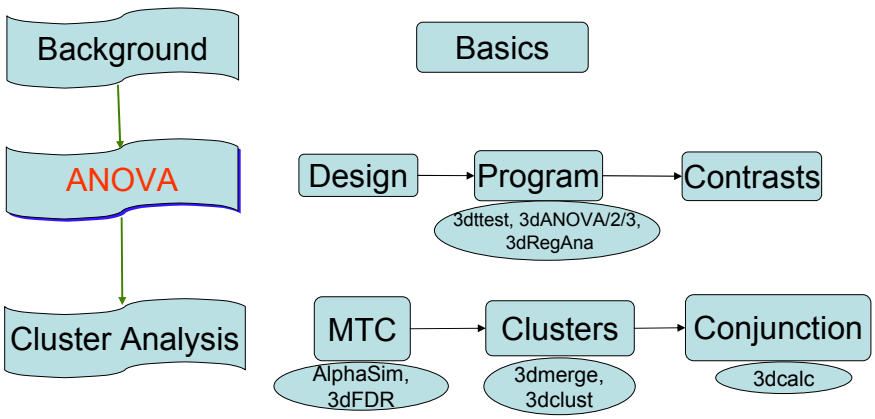
Basics: ANOVA

- More terminology
  - **Main effect**: general info regarding all levels of a factor
  - **Simple effect**: specific info regarding a factor level
  - **Interaction**: mutual/reciprocal influence among 2 or more factors; parallel or not?
  - Disordinal interaction: differences reverse sign
  - Ordinal interaction: one above another
  - **Contrast**: comparison of 2 or more simple effects; coefficients add up to 0
  - **General linear test**



Main effects and interactions in 2-way mixed ANOVA

Group Analysis



Group Analysis: Overview

- Parametric Tests
  - **3dttest** (one-sample, unpaired and paired *t*)
  - **3dANOVA** (one-way between-subject)
  - **3dANOVA2** (one-way within-subject, 2-way between-subjects)
  - **3dANOVA3** (2-way between-subjects, within-subject and mixed, 3-way between-subjects)
  - **3dRegAna** (regression/correlation, unbalanced ANOVA, ANCOVA)
  - GroupAna (Matlab script for up to 5-way ANOVA)
- Non-Parametric Analysis
  - No assumption of normality; Statistics based on ranking
  - Appropriate when number of subjects too few
  - Programs
    - **3dWilcoxon** (~ paired *t*-test)
    - **3dMannWhitney** (~ two-sample *t*-test)
    - **3dKruskalWallis** (~**3dANOVA**)
    - **3dFriedman** (~**3dANOVA2**)
    - Permutation test: plugin on AFNI under Define Datamode / Plugins /
  - Can't handle complicated designs
  - Less sensitive to outliers (more robust) and less flexible than parametric tests

Group Analysis: Overview

- How many subjects?
  - Power: proportional to $\sqrt{n}$; $n > 10$
  - Efficiency increases by the square root of # subjects
  - Balance: Equal number of subjects across groups if possible
- Input
  - % signal change (**not** statistics)
    - HRF magnitude: Regression coefficients
    - Contrast
  - Common brain in tlrc space
    - Resolution: Doesn't have to be 1x1x1 mm^3
- Design
  - Number of factors
  - Number of levels for each factor
  - Within-subject / repeated-measures vs. between-subjects
    - Fixed (factors of interest) vs. random (subject)
    - Nesting: Balanced?
  - Which program?
- Contrasts
  - One-tail or two-tail?

Group Analysis : `3dttest`

- Basic usage
  - One-sample *t*
    - One group: simple effect
    - Example: 15 subjects under condition *A* with H_0: $\mu_A = 0$
  - Two-sample *t*
    - Two groups: Compare one group with another
    - ~ 1-way between-subject (**`3dANOVA2 -type 1`**)
    - Unequal sample sizes allowed
    - Assumption of equal variance
    - Example: 15 subjects under *A* and 13 other subjects under *B* - H_0: $\mu_A = \mu_B$
  - Paired *t*
    - Two conditions of one group: Compare one condition with another
    - ~ one-way within-subject (**`3dANOVA2 -type 3`**)
    - ~ one-sample *t* on individual contrasts
    - Example: Difference between conditions A and B for 15 subjects with H_0: $\mu_A = \mu_B$
- Output: 2 values (% and *t*)
- Versatile program: Most tests can be done with **`3dttest`**: piecemeal vs. bundled

Group Analysis: `3dANOVA`

- Generalization of two-sample *t*-test
  - One-way between-subject
  - H_0: no difference across all levels (groups)
  - Examples of groups: gender, age, genotype, disease, *etc.*
  - Unequal sample sizes allowed
- Assumptions
  - Normally distributed with equal variances across groups
- Results: 2 values (% and *t*)
- **`3dANOVA`** vs. **`3dttest`**
  - Equivalent with 2 levels (groups)
  - More than 2 levels (groups): Can run multiple two-sample *t*-test

- **Group Analysis**: **3dANOVA2**
  - Designs
    - One-way within-subject (**type 3**)
      - Major usage
      - Compare conditions in one group
      - Extension and equivalence of paired *t*
    - Two-way between-subjects (**type 1**)
      - 1 condition, 2 classifications of subjects
      - Extension and equivalence two-sample *t*
      - Unbalanced designs disallowed: Equal number of subjects across groups
  - Output
    - Main effect (**-fa**): *F*
    - Interaction for two-way between-subjects (**-fab**): *F*
    - Contrast testing
      - Simple effect (**-amean**)
      - 1st level (**-acontr, -adiff**): among factor levels
      - 2nd level (interaction) for two-way between-subjects
      - 2 values per contrast: % and *t*

- **Group Analysis**: **3dANOVA3**
  - Designs
    - Three-way between-subjects (**type 1**)
      - 3 categorizations of groups
    - Two-way within-subject (**type 4**): Crossed design AXBXC
      - Generalization of paired *t*-test
      - One group of subjects
      - Two categorizations of conditions: A and B
    - Two-way mixed (**type 5**): Nested design BXC(A)
      - Two or more groups of subjects (Factor A): subject classification, e.g., gender
      - One category of condition (Factor B)
      - Nesting: balanced
  - Output
    - Main effect (**-fa and -fb**) and interaction (**-fab**): *F*
    - Contrast testing
      - 1st level: **-amean, -adiff, -acontr, -bmean, -bdiff, -bcontr**
      - 2nd level: **-abmean, -aBdiff, -aBcontr, -Abdiff, -Abcontr**
      - 2 values per contrast : % and *t*

Group Analysis: GroupAna

- Multi-way ANOVA
  - Matlab script package for up to 5-way ANOVA
  - Requires Matlab plus Statistics Toolbox
  - GLM approach (slow)
  - Powerful: Test for interactions
  - Downside
    - Difficult to test and interpret simple effects/contrasts
    - Complicated design, and compromised power
  - Heavy duty computation: minutes to hours
    - Input with lower resolution recommended
    - Resample with **`adwarp -dxyz #`** and **`3dresample`**
  - Can handle both volume and surface data
  - Can handle following unbalanced designs (two-sample *t* type):
    - 3-way ANOVA type 3: BXC(A)
    - 4-way ANOVA type 4: BXCXD(A)
    - 4-way ANOVA type 4: CXD(AXB)
- See http://afni.nimh.nih.gov/sscc/gangc for more info

Group Analysis: Example

- Design
  - 4 conditions (TM, TP, HM, HP) and 8 subjects
  - 2-way within-subject: 2x2x8
    - A (Object), 2 levels: Tool vs Human
    - B (Animation), 2 levels: Motion vs Point
    - C (subject), 8 levels
    - AxBxC: Program?

      `3dANOVA3 -type 4`
- Main effects (A and B): 2 *F* values
- Interaction AXB: 1 *F*
- Contrasts
  - 1st order: TvsH, MvsP
  - 2nd order: TMvsTP, HMvsHP, TMvsHM, TPvsHP
  - 6x2 = 12 values
- Logistic
  - Input: 2x2x8 = 32 files (4 from each subject)
  - Output: 18 subbricks

• Group Analysis: Example

- Script

```
3dANOVA3 -type 4  -alevels 2  -blevels 2  -clevels 8 \

-dset 1 1 1 ED_TM_irf_mean+tlrc \
-dset 1 2 1 ED_TP_irf_mean+tlrc \
-dset 2 1 1 ED_HM_irf_mean+tlrc \
-dset 2 2 1 ED_HP_irf_mean+tlrc \
…
-adiff    1  2 TvsH1 \  (indices for difference)
-acontr   1 -1 TvsH2 \  (coefficients for contrast)
-bdiff    1  2 MvsP1 \
-aBdiff   1  2 : 1 TMvsHM \  (indices for difference)
-aBcontr  1 -1 : 1 TMvsHM \  (coefficients for contrast)
-aBcontr -1  1 : 2 HPvsTP \
-Abdiff   1 : 1  2 TMvsTP \
-Abcontr  2 : 1 -1 HMvsHP \

-fa  ObjEffect \
-fb  AnimEffect \
-fab ObjXAnim \

-bucket Group
```

Model type, number of levels for each factor

Input for each cell in ANOVA table: totally 2X2X8 = 32

1st order Contrasts, paired *t* test

2nd order Contrasts, paired *t* test

Main effects & interaction *F* test; Equivalent to contrasts

Output: bundled

• Group Analysis: Example

- Alternative approaches
  - GroupAna
  - Paired *t*: 6 tests
    - Program: `3dttest -paired`
    - For TM vs HM: 16 (2x8) input files (β coefficients: %) from each subject

```
3dttest -paired -prefix TMvsHM                      \
-set1 ED_TM_irf_mean+tlrc ... ZS_TM_irf_mean+tlrc   \
-set2 ED_HM_irf_mean+tlrc ... ZS_HM_irf_mean+tlrc
```

  - One-sample *t* : 6 tests
    - Program: `3dttest`
    - For TM vs HM: 8 input files (contrasts: %) from each subject

```
3dttest -prefix TMvsHM              \
-base1 0                            \
-set2 ED_TMvsHM_irf_mean+tlrc ... ZS_TMvsHM_irf_mean+tlrc
```

• Group Analysis: ANCOVA

- Why ANCOVA?
  - Subjects might not be an ideally randomized representation of a population
  - If no controlled, cross-subject variability will lead to loss of power and accuracy
  - Direct control: balanced selection of subjects
  - Indirect (statistical) control: untangling covariate effect
  - Covariate: uncontrollable and confounding variable, usually continuous
    - Age
    - Behavioral data, e.g., response time
    - Cortex thickness
    - Gender
- ANCOVA = Regression + ANOVA
  - Assumption: linear relation between % signal change and the covariate
  - GLM approach
  - Avoid multi-way ANCOVA
    - Analyze partial data with one-way ANCOVA
    - Similar to running multiple one-sample or two-sample *t* test
  - **Centralize** covariate so that it would not confound with other effects

• Group Analysis: ANCOVA Example

- Example: Running ANCOVA
  - Two groups: 15 normal vs. 13 patients
  - Analysis: comparing the two groups
  - Running what test?
    - Two-sample *t* with `3dttest`
    - Controlling age effect?
  - GLM model
    - $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} + \varepsilon_i$, i = 1, 2, ..., n (n = 28)
    - Demean covariate (age) X_1
    - Code the factor (group) with a dummy variable

      X_{2i} = { 0, when the subject is a patient; 1, when the subject is normal.
    - With covariate X_1 centralized:

      β_0 = effect of patient; β_1 = age effect (correlation coef); β_2 = effect of normal
    - $X_{3i} = X_{1i} X_{2i}$ models interaction (optional) between covariate and factor (group)

      β_3 = interaction

- **Group Analysis**: ANCOVA Example

```
3dRegAna -rows 28 -cols 3 \

 -workmem 1000 \

 -xydata 0.1 0 0 patient/Pat1+tlrc.BRIK \
 -xydata 7.1 0 0 patient/Pat2+tlrc.BRIK \
 …
 -xydata 7.1 0 0 patient/Pat13+tlrc.BRIK \
 -xydata 2.1 1 2.1 normal/Norm1+tlrc.BRIK \
 -xydata 2.1 1 2.1 normal/Norm2+tlrc.BRIK \
 …
-xydata -8.9 1 -8.9 normal/Norm14+tlrc.BRIK \
 -xydata 0.1 1 0.1 normal/Norm15+tlrc.BRIK \

 -model 1 2 3 : 0 \

 -bucket 0 Pat_vs_Norm \

 -brick 0 coef 0 'Pat' \
 -brick 1 tstat 0 'Pat t' \
 -brick 2 coef 1 'Age Effect' \
 -brick 3 tstat 1 'Age Effect t' \
 -brick 4 coef 2 'Norm-Pat' \
 -brick 5 tstat 2 'Norm-Pat t' \
 -brick 6 coef 3 'Interaction' \
 -brick 7 tstat 3 'Interaction t'
```

Model parameters: 28 subjects, 3 independent variables

Memory

Input: Covariates, factor levels, interaction, and input files

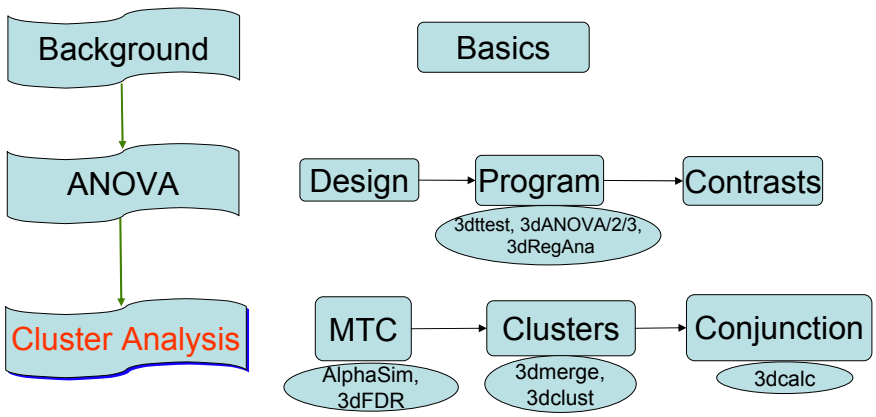
Specify model for F and R^2

Output: #subbriks = 2*#coef + F + R^2

Label output subbricks

See http://afni.nimh.nih.gov/sscc/gangc/ANCOVA.html for more information

Group Analysis



• Cluster Analysis: Multiple testing correction

- 2 types of errors in statistical tests
  - What is H_0 in FMRI studies?
  - Type I = P (reject H_0|when H_0 is true) = false positive = p value
    Type II = P (accept H_0|when H_1 is true) = false negative = β
  - Usual strategy: controlling type I error
    (power = 1- β = probability of detecting true activation)
  - Significance level = α: $p < \alpha$
- Family-Wise Error (FWE)
  - Birth rate H_0: sex ratio at birth = 1:1
    - What is the chance there are 5 boys (or girls) in a family?
    - Among100 families with 5 kids, expected #families with 5 boys =?
  - In fMRI H_0: no activation at a voxel
    - What is the chance a voxel is mistakenly labeled as activated (false +)?
    - Multiple testing problem: With n voxels, what is the chance to mistakenly label at least one voxel? *Family-Wise Error*: $\alpha_{FW} = 1-(1-p)^n \rightarrow 1$ as n increases
    - Bonferroni correction: $\alpha_{FW} = 1-(1-p)^n \sim np$, if $p << 1/n$
      Use $p=\alpha/n$ as individual voxel significance level to achieve $\alpha_{FW} = \alpha$

• Cluster Analysis: Multiple testing correction

- Multiple testing problem in fMRI: voxel-wise statistical analysis
  - Increase of chance at least one detection is wrong in cluster analysis
  - 3 occurrences of multiple testing: individual, group, and conjunction
  - Group analysis is the most concerned
- Two approaches
  - Control FWE: $\alpha_{FW} = P$ (≥ one false positive voxel in the whole brain)
    - Making α_{FW} small but without losing too much power
    - Bonferroni correction doesn't work: $p=10^{-8}$~10^{-6}
      *Too stringent and overly conservative: Lose statistical power
    - Something to rescue? Correlation and structure!
      *Voxels in the brain are not independent
      *Structures in the brain
  - Control false discovery rate (FDR)
    - FDR = expected proportion of false + voxels among all detected voxels
  - Concrete example: individual voxel p = 0.001 for a brain of 25,000 EPI voxels
    - Uncorrected → 25 false + voxels in the brain
    - FWE: corrected p = 0.05 → 1 false + among 20 brains for a fixed voxel location
    - FDR: corrected p = 0.05 → 5% voxels in those positively labeled ones are false +

Cluster Analysis: `AlphaSim`

- FWE: Monte Carlo simulations
  - Named for Monte Carlo, Monaco, where the primary attractions are casinos
  - Program: **`AlphaSim`**
    - Randomly generate some number (e.g., 1000) of brains with random noise
    - Count the proportion of voxels are false + in all brains
    - Parameters:
      - * ROI
      - * Spatial correlation
      - * Connectivity
      - * Individual voxel significant level (uncorrected *p*)
    - Output
      - * Simulated (estimated) overall significance level (corrected *p*-value)
      - * Corresponding minimum cluster size
    - Decision: Counterbalance among
      - * Uncorrected *p*
      - * Minimum cluster size
      - * Corrected *p*

Cluster Analysis: `AlphaSim`

- Example

```
AlphaSim \
-mask MyMask+orig \
-fwhmx 4.5 -fwhmy 4.5 -fwhmz 6.5 \
-rmm 6.3 \
-pthr 0.0001 \
-iter 1000
```

Program

Restrict correcting region: ROI

Spatial correlation

Connectivity: how clusters are defined

Uncorrected *p*

Number of simulations

- Output: 5 columns
  - Focus on the 1st and last columns, and ignore others
  - 1st column: minimum cluster size in voxels
  - Last column: alpha (α), overall significance level (corrected *p* value)

Cl Size	Frequency	Cum Prop	p/Voxel	Max Freq	Alpha
2	1226	0.999152	0.00509459	831	0.859
3	25	0.998382	0.00015946	25	0.137
4	3	1.0	0.00002432	3	0.03

  - May have to run several times with different uncorrected *p*: uncorrected p↑↔ cluster size↑

Cluster Analysis: 3dFDR

	Declared Inactive	Declared Active	
Truly Inactive	N_{ii}	N_{ia} (I)	T_i
Truly Active	N_{ai} (II)	N_{aa}	T_a
	D_i	D_a	

- Definition:

  FDR = proportion of false + voxels among all detected voxels

$$FDR = \frac{N_{ia}}{D_a} = \frac{N_{ia}}{N_{ia} + N_{aa}}$$

- Doesn't consider
  - spatial correlation
  - cluster size
  - connectivity
- Again, only controls the **expected** % false positives among declared active voxels
- Algorithm: statistic (*t*) ➔ *p* value ➔ FDR (*q* value) ➔ *z* score
- Example:

```
3dFDR -input 'Group+tlrc[6]'      \
   -mask_file mask+tlrc           \
   -cdep -list                    \
   -output test
```

One statistic

ROI

Arbitrary distribution of *p*

Output

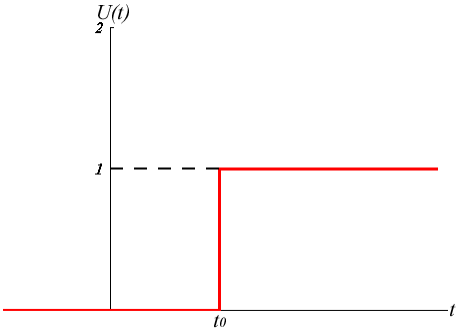
Cluster Analysis: FWE or FDR?

- Correct type I error in different sense
  - FWE: $\alpha_{FW} = P$ (≥ one false positive voxel in the whole brain)
    - Frequentist's perspective: Probability among many hypothetical activation brains
    - Used usually for parametric testing
  - FDR = expected % false + voxels among all detected voxels
    - Focus: controlling false + among detected voxels in one brain
    - More frequently used in non-parametric testing
- Fail to survive correction?
  - At the mercy of reviewers
  - Analysis on surface
  - Tricks
    - One-tail?
    - ROI – cheating?
  - Many factors along the pipeline
    - Experiment design: power?
    - Sensitivity vs specificity
    - Poor spatial alignment among subjects

• Cluster Analysis: Conjunction analysis

- Conjunction analysis
  - Common activation area
  - Exclusive activations
- Double/dual thresholding with AFNI GUI
  - Tricky
  - Only works for two contrasts
  - Common but not exclusive areas
- Conjunction analysis with `3dcalc`
  - Flexible and versatile
  - **Heaviside unit (step function)** defines a *On/Off* event

$$U(t-t_0)=\begin{cases}1 & t\geq t_0\\ 0 & t<t_0\end{cases}$$



• Cluster Analysis: Conjunction analysis

- Example with 3 contrasts: A vs D, B vs D, and C vs D
  - Map 3 contrasts to 3 numbers: A > D: 1; B > D: 2; C > D: 4 (why 4?)
  - Create a mask with 3 subbricks of *t* (all with a threshold of 4.2)

```
3dcalc -a func+tlrc'[5]' -b func+tlrc'[10]' -c func+tlrc'[15]' \
-expr 'step(a-4.2)+2*step(b-4.2)+4*step(c-4.2)' \
-prefix ConjAna
```

  - 8 (=2^3) scenarios:
    0: none;
    1: A > D but no others;
    2: B > D but no others;
    3: A > D and B > D but not C > D;
    4: C > D but no others;
    5: A > D and C > D but not B > D;
    6: B > D and C > D but not A > D;
    7: A > D, B > D and C > D

Miscellaneous

- Fixed-effects analysis
- Sphericity and Heteroscedasticity
- Trend analysis
- Correlation analysis (aka functional connectivity)

Need Help?

- Command with "-help"
  - `3dANOVA3 -help`
- Manuals
  - http://afni.nimh.nih.gov/afni/doc/manual/
- Web
  - http://afni.nimh.nih.gov/sscc/gangc
- Examples: HowTo#5
  - http://afni.nimh.nih.gov/afni/doc/howto/
- Message board
  - http://afni.nimh.nih.gov/afni/community/board/
- Appointment

Contact us @1-800-NIH-AFNI